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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1651	17

DATE MAILED: 01/28/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 11/22/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-9, 11, 12 and 14-22 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-9, 11, 12 and 14-22 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLL WING PAGES –

★ U.S. GPO: 1998-410-238/40050

The amendment of 11/22/99 has been entered. The amendment amended claims 11, 12, 14-18, 21 and 22.

The amendments to claims 21 and 22 have not been entered since "composition" is not recited in line 1 of these claims. See lines 1 and 2 on page 3 of the previous office action of 8/17/99 where these claims are rejected under 35 U.S.C. 112, second paragraph.

Claims examined on the merits are 1-9, 11, 12 and 14-22 which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As set forth in the previous office action, these claims are confusing and unclear by reciting "The method of claim 18" since claim 18 is drawn to a composition.

Claims 1, 3-8, 11, 14-19 and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Atala et al (Journal of Urology) (presented at annual meeting on Oct. 10-15, 1992) for the type of reasons set forth in the previous office action of 8/17/99.

The claims are drawn to a method and implant for introducing cells into an animal to form tissue wherein a solution of a biodegradable, biocompatible natural or synthetic organic polymer, which is capable of hardening into a three-dimensional open-lattice structure which entraps water molecules to form a hydrogel, is mixed with dissociated cells to

form a cell-polymeric composition, and the composition is introduced into an animal.

Atala et al disclose preparing an injectable alginate solution containing chondrocytes and injecting the solution to form tissue *in vivo*.

Applicants have presented a 37 C.F.R. 1.132 Declaration in accordance with *In re Katz*, USPQ 14,18 (CCPA 1982) to overcome Atala et al. However, the declaration is directed to an abstract by Atala et al entitled "Cartilage Cells as a Potential Treatment for Reflux" which is asserted to contain three authors, whereas the reference cited is a publication by Atala et al entitled "Injectable Alginate Seeded with Chondrocytes as a Potential Treatment for Vescoureteral Reflux" which contains seven authors. If only the abstract and not the publication cited was available to the public at the annual meeting in 1992, this should have been stated in the declaration. Also, the publication contains Wooseob Kim and Joseph P. Vacanti in addition to Alan B. Retik as co-authors not listed as inventors. Were the authors of the abstract only Charles Vacanti, Anthony Atala and Alan B. Retik? If Wooseob Kim and Joseph P. Vacanti are also authors of the abstract, the declaration does not mention whether or not these authors are inventors. Additionally, if Linda G. Cima, who is an author of the publication and an inventor, is not an author of the abstract, the authorship entity of the abstract is different from the inventive entity even if Alan B. Retik is not an inventor. If the paper presented at the annual meeting is not the Atala et al publication cited that has seven authors, this should be

established, and a copy of the paper showing its authorship presented to the public at the annual meeting should be supplied.

Claims 2, 9, 12, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atala et al in view of Nevo et al (4,642,120) and Vacanti et al (5,041,138), and if necessary in further view of Vacanti et al (J. Ped. Surg.)(newly applied).

Claims 2 and 12 require the cell-polymeric composition to be hardened before introduction into an animal, and claim 9 requires hardening while the composition is in a mold to obtain an anatomical shape. Claims 20 and 22 require the cells to be osteoblasts.

Nevo et al disclose (col 1, lines 5-10 and col 3, lines 62-68) repairing cartilage or bone by implanting a gel containing chondrocytes or bone marrow stem cells .

Vacanti et al ('138) disclose forming a molded matrix containing chondrocytes for implanting to form cartilage (col 3, lines 17-43).

Vacanti et al (J. Ped. Surg.) disclose forming a polymer-cell scaffold for implanting wherein a desired shape of the polymer scaffold may be obtained by solvent casting or compression molding (page 3, right col).

It would have been obvious to gel the chondrocyte-containing alginate solution of Atala et al in a mold to provide a desired shape, and then implant the shaped gel as suggested by Nevo et al implanting a gel containing cells to repair a defect and Vacanti et al ('138), and if needed Vacanti et al (J. Ped. Surg.), disclosing implanting molded scaffolds containing cells. When desiring to repair bone as suggested by

Nevo et al, the use of osteoblasts as the cells would have been obvious since these are known bone forming cells.

The comments set forth above in regard to the declaration and Atala et al also apply to this rejection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 4-8, 11, 12, 14-18, 20 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Schlameus et al (5,294,446) (newly applied).

Schlameus et al disclose mixing osteoprogenitor cells with a solution of alginate, gelling the alginate to form microcapsules containing the cells and implanting the microcapsules to regenerate bone (col 3, lines 51-68, and col 4, lines 30-40).

The present claims encompass mixing cells with an alginate solution to form a cell-alginate composition, and gelling the alginate to from microcapsules as disclosed by Schlameus et al.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schlameus et al in view of Barry et al (5,266,326) and Dionne et al (WO 92/19195), and if necessary in further view of Bhatnagar (5,354,736) (all newly applied).

The claim requires hardening the cell-polymeric composition after introduction into an animal.

Schlameus et al is described above.

Berry et al disclose (abstract and col 3, lines 40-45) injecting an alginate solution and a calcium chloride solution into intra-articular space following closure of a surgical site, and allowing the alginate to gel *in situ* to prevent intra-articular adhesions. The alginate solution may contain drugs and other therapeutic agents (col 6, lines 52-55).

Dionne et al disclose (page 4, lines 5-16) forming an implantable vehicle containing cells by immobilizing cells in a hydrogel matrix core and surrounding the core with a jacket or membrane that is permselective and prevents the cells in the core from immunological attack. The core and membrane can be made of the same composition hydrogel (page 9, lines 21-22) and can be alginate cross-linked with calcium ions (page 9, lines 3-6, and page 18, line 10). It is possible for a single, continuous hydrogel matrix to provide both immunoisolation and support or immobilization (page 53, lines 5-24). It is further disclosed (page 18, lines 18-24) that a hydrogel matrix precursor solution can be included but not exposed to polymerizing conditions. In the case of sodium alginate, a hydrogel will form after implantation as calcium ions are scavenged from surrounding tissues.

Bhatnagar discloses (abstract and col 13, lines 45-49) carrying out soft and hard tissue repair by implanting a hydrogel matrix that promotes cell attachment to the matrix and cell migration into the matrix. The hydrogel matrix results in a three dimensional environment that causes cells to differentiate (col 13, lines 50-55). When soft tissue repair is

carried out, injection can be prior to gelation and the gel formed in situ (col 13, lines 58-60).

It would have been obvious to omit forming microcapsules and inject the cell-containing alginate solution of Schlameus et al into intra-articular space as suggested by Berry et al to allow *in situ* gel formation to prevent intra-articular adhesions, and as suggested by Dionne et al disclosing forming an alginate hydrogel containing cells after implantation as calcium ions are scavenged from surrounding tissues as an alternative to forming an alginate gel matrix containing cells and implanting the matrix. If needed, further suggestion is provided by Bhatnagar disclosing forming a hydrogel *in situ* for tissue repair. The disclosure by Berry et al that drugs or other therapeutic agents can be in the injected alginate solution would have suggested that the cells of Schlameus et al can be present in the alginate solution when injected to obtain the tissue repair function of the cells in addition to preventing adhesions as disclosed by Berry et al.

Claims 9, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schlameus et al in view of Nevo et al (4,642,120) and Vacanti et al (5,041,138), and if necessary in further view of Vacanti et al (J. Ped. Surg.).

Claim 9 requires the cell-polymeric composition to be formed into a desired anatomical shape in a mold prior to introduction into an animal, and claims 19 and 21 require the cells to be chondrocytes.

The references are described above.

It would have been obvious to form the alginate gel of Schlameus et al into a molded anatomical shape instead of microcapsules as suggested

by Nevo et al implanting a gel containing cells that is not in the form of microcapsules and by Vacanti et al ('138), and if needed Vacanti et al (J. Ped. Surg.), disclosing implanting molded scaffolds containing cells. Nevo et al and Vacanti et al ('138) use chondrocytes as the cells implanted, and it would have been obvious to implant these cells for their known cartilage forming function.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is (703) 308-0520. The examiner can normally be reached on Monday-Thursday and every other Friday from about 8:30 AM to about 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, a message can be left on voice mail.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn, can be reached at telephone number (703) 308-4743.

The fax phone number is (703) 305-3014 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 1651

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1/27/00